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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/517,154	07/11/2005	Ryuichi Morishita	6235-69895-01	2664

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EXAMINER

NOBLE, MARCIA STEPHENS

ART UNIT PAPER NUMBER

1632

DATE MAILED: 11/15/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

10/517,154

Applicant(s)

MORISHITA ET AL.

Examiner

Marcia S. Noble

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on 08 September 2006.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1, 3, 6 and 12-15 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1, 3, 6 and 12-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SI/08)  
Paper No(s)/Mail Date 3/7/2005
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Preliminary Matters***

1. The instant application has been transferred to a new Examiner. The new examiner is Marcia Noble.

### ***Status of Claims***

2. Claims 1, 3, 6, and 12-15 are pending. Claims 2, 4, 5, and 7-11 were previously canceled. Claims 1, 6, and 13 are amended by Applicant's response to second Non-Final Rejection, filed 5/11/2006. Claims 1, 3, 6, and 12-15 are under consideration.

### ***Claim Objections***

3. Amended claims 1 and 6 objected to because of the following informalities:

The instant claims recite "Japan (HVJ)", which that HVJ is an abbreviation for Japan and therefore from the claim alone, it is unclear if the claims is suggesting a Japan envelope or an HVJ envelope. Specification clarifies the issue the HVJ is a hemagglutinating virus of Japan (p. 4, lines8). However to clarify the claims, appropriate correction is required.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct

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from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1, 3, 6, and 12-15 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 2, 4, and 5 of U.S. Patent No. 6,936,594 (of record) in view of Hayashi et al (Gene Therapy 8:1167-1173, 2001, IDS) and Barnes et al (J Lipid Res 28:130-137, 1987).

The instant rejection was made of the grounds that the "HVJ-envelop" of the instant application would not be structurally distinguishable from the "HVJ-liposome" of the '594 because they both comprise DNA encoding HGF, phosphatidylserine, phosphatidylcholine, and cholesterol (p. 4 of Non-Final Rejection, mailed 5/11/06).

Applicant traversed this rejection on the grounds that there is a significant difference between an HVJ envelope and a liposome. They further cite Barnes et al stating that the HVJ envelope also has two integral membrane glycoproteins, HN and F, that project from the viral surface, and further suggest that a liposome does not have these glycoproteins and that the claims have been amended to recite "liposome-free".

These arguments are not found persuasive because the final product in the instant invention would not be structurally distinguishable from the HVJ-liposome of the '594. It is acknowledged that a liposome in itself would not encompass the HN and F glycoproteins. However, the HVJ-liposome is composite of a liposome and an inactivated HVJ virus which provides the HVJ envelope (see [38] and [39] of '594). Therefore, this would result in HVJ envelope comprising phosphatidylserine, phosphatidylcholine, and cholesterol of its own and other HVJ factor and phosphatidylserine, phosphatidylcholine, and cholesterol from the liposome. However, the phosphatidylserine, phosphatidylcholine, and cholesterol from the liposome and the HVJ envelope would not be structurally distinguishable. Therefore absence evidence to the contrary the HVJ-liposome and the HVJ-envelope of the instant invention would be structurally indistinguishable. Furthermore, since the two structures may be made differently they end up being the same indistinguishable product, therefore the amendment to the claims requiring that it be liposome free does not overcome this rejection because the liposome starting material would be indistinguishable from the HVJ envelope once the composite is made. Since the amendments and arguments by Applicant do not overcome the rejection, the instant rejection is maintained.

***Claim Rejections - 35 USC § 112, 1<sup>st</sup> Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

***New Matter***

5. Claims 1, 3, 6, and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

The instant claims recite, "free of liposome". However, the specification provides no literal or figurative support for "free of liposome". Applicant specifies that p 12, 13-18, and 30 of the specification provide support for "free of liposome". However, p. 12, 13-18, and 30 does not require the intact envelope and p18 provides for purification of the envelope, which does not provide support to support the term, "free of liposome".

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, claims 1, 3, 6, and 12-15 are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

The specification teaches that an alternative to methods using viral vectors, in vivo gene transfers methods using liposomes together with viral outer membranes, or HIV liposome mediated gene transfer methods can be used (p. 4, lines 7-9). The

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specification also teaches HVJ-liposome are made by fusing HVJ virions with liposomes (p. 4, lines 19-20). The specification also teaches that viral envelope vector, which is an inactivated virus can serve as a vector for gene transfer (p. 4, lines 28-31). However, this does not suggest that any of the vectors are free of liposome, which in its broadest interpretation is a lipid bilayer and therefore the specification lack specific guidance to teach an artisan how to make the instant vector "free of liposome".

MPEP 2163.06 notes "If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981)." MPEP 2163.02 teaches that "Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application. MPEP 2163.06 further notes "When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure".

***New Scope of Enablement Rejection***

6. Claims 6, 12, 14, and 15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for reducing the infarction area of an induced cerebral infarction comprising (1) administering by direct administration into the subarachnoid space of an animal model an agent comprising a HVJ-envelope vector comprising an isolated nucleic acid encoding a hepatocyte growth factor (HGF) operably linked to a promoter that drives expression of the nucleic acid encoding a HGF and (2) inducing a cerebral infarction in an animal model, wherein said administration results in a reduction of the infarcted area, does not reasonably provide enablement for a method for reducing an infarcted of a natural causes infarction comprising administering an agent comprising and HVJ envelope vector by direct injection into the subarachnoid space of any subject prior to the occurrence of said cerebral infarction wherein the HVJ envelope vector comprises an isolated nucleic acid encoding a HGF protein only enclosed within an HVJ-envelope and is free of liposome. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the



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factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue".

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

The specification discloses in Example 3 (p. 18) a method of administering to the subarachnoid space of a rat a HJV envelope vector comprising a nucleic acid encoding a human HGF gene. Following induced cerebral infarction by carotid artery occlusion in the treated rats, the infarcted regions of the induced cerebral infarction were smaller in those rat treated with the HJV envelop vector containing the nucleic acid encoding HGF compared to those that received an empty vector (Figure 4).

The basis of the instant rejection lies in the recitation of administering an agent for treatment of a cerebral infarction to a "subject prior to the occurrence of said cerebral infarction". The specification teaches a method of reducing an affected region of infarction in an induced infarction. However, the breadth of the claims encompass treating subjects, which encompasses any animal including humans that have an unanticipated cerebral infarction, which is the real world circumstance of interest. Since

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there is not means by which a cerebral infarction can be predicted in a subject, an artisan would not know how or who to administer the treatment encompassed by the instant claims. Therefore, the instant invention only enabled for methods where an infarction is induced.

Another area of enablement encompasses the minimum structural requirement of a vector to enable function of a vector. The instant claims recite, "vector comprises....an isolated nucleic acid encoding a hepatocyte growth factor protein." However, for a gene therapy agent to be expressed effectively it must minimally comprise the elements to be directed by the transcription and translation machinery of the target cell which require a promoter capable of driving expression in the target cell. Because of the necessity for the minimal elements necessary to drive expression of a gene, an artisan would not know how to use a vector comprising a nucleic acid encoding a hepatocyte growth factor protein, in a gene therapy method that would result in the expression of the therapeutic gene.

Therefore, because the instant claims encompass matter that is not supported by the specification and art, the instant invention is only enabled for a method for reducing the infarction area of an induced cerebral infarction comprising (1) administering by direct administration into the subarachnoid space of an animal model an agent comprising a HVJ-envelope vector comprising an isolated nucleic acid encoding a hepatocyte growth factor (HGF) operably linked to a promoter that drives expression of the nucleic acid encoding a HGF and (2) inducing a cerebral infarction in an animal model, wherein said administration results in a reduction of the infarcted area.

***Claim Rejections - 35 USC § 112, 2<sup>nd</sup> Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claim 13, rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, has been amended to rectify the in clarity and therefore the rejection has been withdrawn.

***New Rejection***

8. Claims 1, 3, 6, and 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Amended claims 1 and 6 recite, "a hemagglutinating virus of Japan (HVJ)-envelope vector". It is unclear if the virus is being claimed or the HVJ-envelope vector. Amended claims 1 and 6 also recite, "free of liposome". The metes and bounds of this recitation are unclear because given its broadest interpretation, a liposome is a lipid bilayer and therefore it is unclear if the claims requiring free of a lipid bilayer.

Claims 3 and 12-15 depend from claims 1 and 6, which have been deemed indefinite. Therefore, dependent claims 3 and 12-15 are rendered indefinite.

***Claim Rejections - 35 USC § 102***

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 1, 3, 6, and 12-15 stand rejected under 35 U.S.C. 102(b) as being anticipated by Morishita et al (Australian Patent Application No. 200073148, published 4/24/2001 now Patent No. 774990; of record) as evidenced by of Hayashi et al (Gene Therapy 8:1167-1173, 2001, IDS) and Barnes et al (J Lipid Res 28:130-137, 1987).

The instant rejection was made of the grounds that the "HVJ-envelop" of the instant application would not be structurally distinguishable from the "HVJ-liposome" of the Morishita because they both comprise DNA encoding HGF, phosphatidylserine, phosphatidylcholine, and cholesterol and therefore Morishita et al anticipates (p. 11 of Non-Final Rejection, mailed 5/11/06).

Applicant traversed this rejection on the grounds that there is a significant difference between an HVJ envelope and a liposome. They further cite Barnes et al stating that the HVJ envelope also has two integral membrane glycoproteins, HN and F, that project from the viral surface, and further suggest that a liposome does not have these glycoproteins and that the claims have been amended to recite "liposome-free".

These arguments are not found persuasive for the same reason as described above in the double patenting rejection (see item # 3), and therefore the rejection is maintained.

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7. Claims 1, 3, 6, and 12-15 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hayashi et al (Gene Therapy 8:1167-1173, 2001, IDS) as evidenced by Barnes et al (J Lipid Res 28:130-137, 1987).

The instant rejection was made on the grounds that the "HVJ-envelope" of the instant application would not be structurally distinguishable from the "HVJ-liposome" of the Hayashi et al because they both comprise DNA encoding HGF, phosphatidylserine, phosphatidylcholine, and cholesterol and therefore Hayashi et al anticipates (p. 11 of Non-Final Rejection, mailed 5/11/06).

Applicant traversed this rejection on the grounds that there is a significant difference between an HVJ envelope and a liposome. They further cite Barnes et al stating that the HVJ envelope also has two integral membrane glycoproteins, HN and F, that project from the viral surface, and further suggest that a liposome does not have these glycoproteins and that the claims have been amended to recite "liposome-free".

These arguments are not found persuasive for the same reason as described above in the double patenting rejection (see item # 3), and therefore the rejection is maintained.

7. Claims 1, 3, 6, and 12-15 stand rejected under 35 U.S.C. 102(e) as being anticipated by Morishita et al (US Pat No. 6,936,594) as evidenced by Hayashi et al (Gene Therapy 8:1167-1173, 2001, IDS) and Barnes et al (J Lipid Res 28:130-137, 1987).

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The instant rejection was made on the grounds that the "HVJ-envelop" of the instant application would not be structurally distinguishable from the "HVJ-liposome" of the Hayashi et al because they both comprise DNA encoding HGF, phosphatidylserine, phosphatidylcholine, and cholesterol and therefore Hyashi et al anticipates (p. 12 f Non-Final Rejection, mailed 5/11/06).

Applicant traversed this rejection on the grounds that the amendments of claims 1 and 6 distinguish the invention from Morishita.

These arguments are not found persuasive for the same reason as described above in the double patenting rejection (see item # 3), and therefore the rejection is maintained.

8. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Marcia S. Noble whose telephone number is (571) 272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Marcia S. Noble

Joe Winters  
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